REMARKS

Amendments to the Claims

With this amendment, claims 1-15 and 17-28 are pending. Claims 1, 8-12, and 17-19 have been amended. Claims 2-7, 13-15, and 20-25 have been withdrawn as drawn to a non-elected invention. Claim 16 has been canceled without prejudice or disclaimer. New claims 26-28 have been added.

Claims 8-12 and 19 have been amended merely to correct matters of formality. Claims 17 and 18 have been amended to correct their dependencies and to correct matters of formality. Claim 1 has been amended to recite "[a] method of identifying a candidate phosphatase and tensin homolog (PTEN) pathway modulating agent, said method comprising the steps of: (a) providing a first assay system comprising a microtubule affinity regulating kinase (MARK) nucleic acid selected from the group consisting of SEQ ID NOs: 1-13 or a functionally active fragment or derivative thereof, wherein the functionally active fragment or derivative has kinase activity; (b) contacting the first assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; (c) detecting a test agent-biased activity of the first assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate PTEN pathway modulating agent; (d) confirming that the test agent of (b) is a candidate PTEN pathway modulating agent by providing a second assay system comprising cultured cells or a non-human animal expressing MARK, wherein the second assay system measures a change in the PTEN pathway; (e) contacting the second assay system with the test agent of (b); and (f) determining a change in the PTEN pathway in the second assay system, wherein a change in the PTEN pathway between the presence and absence of said test agent confirms the test agent as a candidate PTEN pathway modulating agent". Support for the amendments to claim 1 is found throughout the specification, for example, at pages 5, 6, 20, 24-27, and 30-31.

New claim 26 recites "[t]he method of claim 1, wherein the first assay system comprises cultured cells that express a MARK polypeptide encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 1-13 or a functionally active

fragment or derivative thereof, wherein the functionally active fragment or derivative has kinase activity." Support for new claim 26 is found throughout the specification, for example, at pages 5, 20-27, 30-31, and 40-41.

New claim 27 depends from claim 26 and further recites that the cultured cells additionally have defective PTEN function. Support for new claim 26 is found throughout the specification, for example, at page 25.

New claim 28 depends from claim1 and recites that the second assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system. Support for new claim 28 is found throughout the specification, for example, at pages 4-5, 24-25, 26, and 27.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. No new matter has been added by way of these amendments.

Restriction Requirement

Applicants submit that new claims 26-28 read on the elected invention. Thus, claims 1, 8-12, 17-19, and 26-28 read on the elected invention. If the Office considers new claim 28 to recite more than one species, Applicants elect a cell proliferation assay for prosecution. Upon allowance of the generic claim, Applicants are entitled to consideration of the additional species. The claims readable on the elected species are claims 1, 8-11, 17, and 26-28.

Claim Objections

Claims 1, 8-12, and 16-19 were objected to because the abbreviations PTEN, MARK, and PMO were recited. Claims 1 and 10 have been amended to recite the full names of PTEN, MARK, and PMO, thereby obviating the objections to claims 1, 8-12, and 16-19. Applicants respectfully request withdrawal of these claim objections.

Claims 1, 8-12, and 16-19 were objected to for reciting non-elected subject groups, i.e., MARK polypeptide inhibitors. Claim 1 has been amended to delete reference to the use

of a MARK polypeptide in the method thereby obviating the objections to claims 1, 8-12, and 16-19. Applicants respectfully request withdrawal of these claim objections.

35 USC § 112, Second Paragraph Rejections

Claims 1,8-12, and 16-19 were rejected under 35 USC 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse the rejections.

The Office rejected claims 1 and 8-12 for being indefinite, however, the Office failed to provide the specific reason(s) for the rejection. Applicants respectfully request clarification of the 35 USC §112, second paragraph, rejections of claims 1 and 8-12.

The Office alleged that claims 16-19 are indefinite because it is not clear what kind of assay the recited second assay system is and thus it is not clear what is encompassed by the claims. Claim 16 has been canceled, thus rendering the rejection moot as to claim 16. Claim 1 has been amended to include the method steps of original claim 16 and further amended to clarify that the second assay system is an assay system that measures a change in the PTEN pathway. Thus, the recited second assay system is either a cell culture assay or non-human animal model assay in which the cultured cells or non-human animal express MARK, wherein the assay system measures a change in the PTEN pathway. The specification provides numerous examples of assays that can be used to measure a change in the PTEN pathway in cultured cells and in animal models, including, for example, apoptosis assays, cell proliferation assays, angiogenesis assays, and neovascularization assays. Accordingly, Applicants believe that the claims as amended are clear and respectfully request withdrawal of the 35 USC 112, second paragraph, rejections.

The Office alleged that claims 16-19 are indefinite because it is not clear how one of skill in the art can distinguish between a derivative of a test agent and the agent because the nature of the test agent itself is allegedly not defined. Claim 16 has been canceled, thus rendering the rejection moot as to claim 16. Claim 1 has been amended to include the method steps of original claim 16. Without acceding to the merits of the

rejection, claim 1 does not include the phrase "or agent derived therefrom", thus obviating the rejections. Applicants respectfully request withdrawal of the 35 USC 112, second paragraph, rejections.

35 USC § 112, First Paragraph, Rejections

Claims 1, 8-12, 16-19 were rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Claim 16 has been canceled, thus rendering the rejection moot as to this claim. With respect to claims 1, 8-12, and 17-19, Applicants respectfully traverse the rejections.

The Office argued that the instant claims do not satisfy the written description requirement because allegedly the specification does not provide sufficient recitation of distinguishing identifying characteristics of MARK polynucleotides or describe a sufficient number of representative species of MARK polynucleotides.

In contrast to the Office's allegations, Applicants submit that the instant specification thoroughly describes the claimed methods of identifying a candidate PTEN pathway modulating agent in such a way that would reasonable convey to one skilled in the art that the Applicants had possession of the claimed methods at the time of filing. First, Applicants point out that they are claiming a novel method of using MARK polynucleotides and not the polynucleotides themselves, which polynucleotides are published and known in the art. Second, the specification describes, among other things, the structure, physical and chemical properties, functional characteristics, and methods of making the recited MARK nucleic acid molecules. In addition, the specification provides a sufficient number of representative examples of MARK species. Applicants' disclosure, in combination with MARK polynucleotides known and described in the art, is sufficient to satisfy the written description requirement. Nevertheless, solely in an effort to advance prosecution, claim 1 has been amended to recite a MARK nucleic acid comprising any of SEQ ID NOs: 1-13 or a functionally active fragment thereof, wherein the fragment has kinase activity.

In addition, the Office argued that the claims lack written description because the specification does not describe a link between a MARK polynucleotide and the PTEN

pathway. Specifically, the Office alleged that the specification does not describe how PTEN relates to polynucleotides encoding MARK and does not describe how the function of a defective PTEN can be overcome by expressing a recombinant polynucleotide encoding a MARK.

In contrast to the Office's allegation, the specification describes a link between a MARK polypeptide and the PTEN pathway. For example, the specification at page 1 teaches that PTEN is a tumor suppressor involved in the AKT signaling pathway, which regulates cell proliferation and growth, as well as apoptosis. The specification at page 2 teaches that MARK is protein kinase that phosphorylates microtubule-associated proteins and triggers microtubule disruption. One skilled in art would know that microtubule dispruption is required for cell division and is thus involved in regulation of cell growth and proliferation. The specification at pages 4 and 36 further teaches that MARK is a modifier of the PTEN pathway. In particular, the specification teaches that a genetic screening assay performed in C. elegans specifically identified PAR-1 as a modifier of the PTEN pathway and also teaches that the human ortholog of PAR-1 is MARK.

Furthermore, the specification provides assays and data that demonstrate the link between MARK and the PTEN pathway. On pages 40-41, the specification shows that overexpression of MARK results in cell growth, and RNAi against MARK decreases cell proliferation and growth in cancer cells (ie, cells with defective PTEN phenotype). Further, standard colony assays showed that a decrease in MARK expression results in decreased cell growth and leads to cell apoptosis. In addition, the specification describes a FOXO nuclear translocation assay that assesses involvement of MARK in PTEN/IGF pathway. Reduction of MARK (via RNAi) leads to retention of FOXO in the nucleus, suggesting the involvement of MARK in the PTEN pathway. Thus, the specification fully describes and demonstrates the link between MARK and the PTEN pathway.

With respect to the Office's comment that the specification does not describe how the function of a defective PTEN can be overcome by expressing a recombinant polynucleotide encoding a MARK, Applicants submit that the specification teaches at pages 25 and 33 that defective PTEN results from the over-expression, under-expression, or mis-expression of PTEN. Expression of a MARK polypeptide can inhibit PTEN

expression such that PTEN overexpression is restored to normal levels of expression. More importantly, however, the specification teaches that MARK-modulating agents can specifically bind to and inhibit MARK polypeptides thus restoring PTEN function (pages 3 and 5).

In view of the amendments, Applicants submit that the claims satisfy the written description requirement. Accordingly, Applicants request withdrawal of the 35 USC 112, first paragraph, rejections based on alleged lack of written description.

35 USC § 102(b) Rejections

Claims 1, 8, 11, 16 and 17 have been rejected under 35 USC 102(b), as allegedly being anticipated by Drewes et al. (Cell, 1997, 89:297-308). Claim 16 has been canceled, thus rendering the rejection moot as to this claim. With respect to claims 1, 8, 11 and 17, Applicants respectfully traverse the rejections.

The Office alleges that Drewes et al. anticipates claims 1, 8, 11, 16 and 17 because it allegedly teaches an assay wherein CHO cells were transformed with a vector comprising a polynucleotide that encodes MARK in cells in the presence or absence of taxotere and also allegedly teaches an assay wherein a polynucleotide that encodes MARK was cotransformed with a vector expressing MAP2c, wherein in both assays differential phenotypes of CHO cells were seen.

Under 35 U.S.C. § 102, a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881 (S.D. Ind.1993) ("A patent is anticipated only if all the elements and limitations of the claims are found within a single, prior art reference. No difference may exist between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of invention."); *Structural Rubber Products Co. v. Park Rubber Co.*, 749 F.2d 707, 716 (Fed. Cir. 1984) (All elements of the claimed invention must be contained in a single prior art disclosure and must be arranged in the prior art disclosure as in the claimed invention); M.P.E.P § 2131. The identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d

1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *Chester v. Miller*, 15 USPQ2d 1333 (Fed. Cir. 1990); M.P.E.P. § 2131.

Applicants submit that Drewes et al. does not anticipate the present invention because it fails to teach each and every element as set forth in the claims. Claim 1, as amended, is directed to a method for identifying a candidate PTEN pathway modulating agent, which method comprises (1) providing a first assay system that comprises a MARK nucleic acid selected from the group consisting of SEQ ID NOs: 1-13 or a functionally active fragment or derivative thereof; (2) contacting the first assay system with a test agent; (3) detecting a test agent-biased activity of the first assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as a candidate PTEN pathway modulating agent; (4) confirming that the test agent is a candidate PTEN pathway modulating agent by providing a second assay system that measures a change in the PTEN pathway; (5) contacting the second assay system with the test agent and (6) determining a change in the PTEN pathway in the second assay system, wherein a change in the PTEN pathway between the presence and absence of the test agent confirms the test agent as a candidate PTEN pathway modulating agent.

In contrast, Drewes fails to teach a MARK nucleic acid having a sequence found in any of SEQ ID NOs: 1-13. Thus, Drewes fails to teach a method for identifying a candidate PTEN pathway modulating agent comprising, among other things, a first assay system comprising a MARK nucleic acid selected from the group consisting of SEQ ID NOs: 1-13 or a functionally active fragment or derivative thereof.

Furthermore, Drewes makes no mention whatsoever of the PTEN pathway and thus does not even contemplate a screening assay for identifying a PTEN pathway modulating agent, much less teach an assay which employs the steps of confirming whether the test agent is a candidate PTEN pathway modulating agent by providing a second assay system that measures a change in the PTEN pathway, contacting the second assay system with the test agent, and determining a change in the PTEN pathway in the second assay system, wherein a change in the PTEN pathway between the presence and absence of said test agent confirms the test agent as a candidate PTEN pathway modulating agent.

None of the assays described in Drewes involve measuring a change in the PTEN pathway. Instead, the assays described in Drewes involve measuring the morphological changes associated with expression of MARK in CHO cells in the presence or absence of the MARK modulator taxotere or MAR2c (i.e., observance of smaller and more rounded cells with disrupted microtubules). In the absence of teaching an assay system comprising a MARK nucleic acid selected from the group consisting of SEQ ID NOs: 1-13 and in the absence of teaching an assay that measures changes in the PTEN pathway, Drewes fails to teach each and every step of the claimed invention.

For the reasons set forth above, Drewes does not anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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